Noninvasive Sphenopalatine Ganglion Block for Acute Headache in the Emergency Department: A Randomized Placebo-Controlled Trial

Jason T. Schaffer, MD*; Benton R. Hunter, MD; Kevin M. Ball, BS; Christopher S. Weaver, MD

*Corresponding Author. E-mail: jtschaff@iu.edu, Twitter: @jtschaff.

Study objective: We seek to test the efficacy of noninvasive sphenopalatine ganglion block for the treatment of acute anterior headache in the emergency department (ED) using a novel noninvasive delivery device.

Methods: We conducted a randomized, double-blind, placebo-controlled trial evaluating bupivacaine anesthesia of the sphenopalatine ganglion for acute anterior or global-based headache. This study was completed in 2 large academic EDs. Bupivacaine or normal saline solution was delivered intranasally (0.3 mL per side) with the Tx360 device. Pain and nausea were measured at 0, 5, and 15 minutes by a 100-mm visual analog scale. The primary endpoint was a 50% reduction in pain at 15 minutes. Telephone follow-up assessed 24-hour pain and nausea through a 0- to 10-point verbal scale and adverse effects.

Results: The median reported baseline pain in the bupivacaine group was 80 mm (IQR 66 mm - 93 mm) and 78.5 mm (IQR 64 mm to 91.75 mm) in the normal saline solution group. A 50% reduction in pain was achieved in 48.8% of the bupivacaine group (20/41 patients) versus 41.3% in the normal saline solution group (19/46 patients), for an absolute risk difference of 7.5% (95% confidence interval [CI] −13% to 27.1%). As a secondary outcome, at 24 hours, more patients in the bupivacaine group were headache free (24.7% difference; 95% CI 2.6% to 43.6%) and more were nausea free (16.9% difference; 95% CI 0.8% to 32.5%).

Conclusion: For patients with acute anterior headache, sphenopalatine ganglion block with the Tx360 device with bupivacaine did not result in a significant increase in the proportion of patients achieving a greater than or equal to 50% reduction in headache severity at 15 minutes compared with saline solution applied in the same manner. [Ann Emerg Med. 2015;65:503-510.]

Please see page 504 for the Editor's Capsule Summary of this article.

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INTRODUCTION

Background

Acute headache is a frequent chief complaint in patients presenting to the emergency department (ED), accounting for 1% to 2% of all ED visits.[1,2] The primary goals for the management of headache in the ED are to differentiate the life-threatening causes of headache from benign headache and to relieve headache pain. Although there are effective medications available to relieve headache, oral therapies often fail or are only partially effective, and emergency physicians often resort to intravenous therapies.[3] Common treatments (eg, prochlorperazine, droperidol, metoclopramide) are most effective only when used intravenously and have adverse effects, and some have recently been subject to supply shortages.[3-7] An ideal headache treatment is one that would be fast acting and effective, avoid the need for intravenous access, and have minimal adverse effects.

The sphenopalatine ganglion plays a pivotal role in nociception of headache and facial pain.[8-12] Sphenopalatine ganglion block has been described for treatment of facial and head pain, including cluster headaches, trigeminal neuralgia, and postoperative pain relief for ear, nose, and throat surgeries.[13-17] Recent evidence has implicated the sphenopalatine ganglion as an important neural relay point for common migraine.[8-12] Activation of the sphenopalatine ganglion causes parasympathetic-mediated vasodilation of the cerebral vasculature, producing cephalgia. Anesthetizing

Editor's Capsule Summary

What is already known on this topic

Acute emergency department (ED) headache treatment leaves many with residual symptoms or adverse effects. Sphenopalatine ganglion block is one tool used in select patients.

What question this study addressed

Does a proprietary local anesthetic sphenopalatine ganglion block delivery system allow successful acute ED treatment of anterior or global headache patients?

What this study adds to our knowledge

In a prospective, randomized, placebo-controlled trial of 93 patients, the delivery of bupivacaine did not improve short-term outcomes.

How this is relevant to clinical practice

This study provides no support for using noninvasive sphenopalatine block for acute symptom relief.

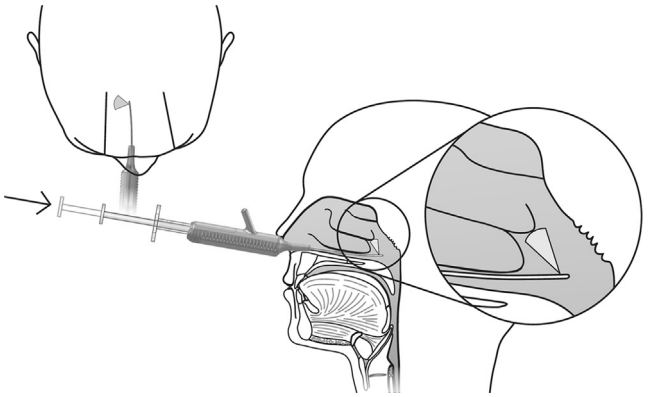

Figure 1. Sphenopalatine ganglion block with the Tx360 device. The device is positioned in the nares as shown, aimed slightly medial and inferior. The attached syringe is advanced into the device, advancing the catheter into the open space in the nasopharynx to the correct location. The medication is then delivered directionally laterally and superiorly to the sphenopalatine ganglion.

the ganglion is thought to attenuate this dilation, resulting in rapid relief of symptoms.[11]

Importance

Conventional techniques for delivering anesthetic to the sphenopalatine ganglion include stereotactic, endoscopic, or fluoroscopic approaches. Direct access to the ganglion is blocked by its location deep in the nasopharynx in a recess posterior to the middle turbinate. This makes transnasal approaches difficult and unreachable by a simple cotton-tip applicator. Other transnasal approaches are imperfect and classically combined with recumbent position, larger volumes and time, or fluoroscopy.[18,19] The difficulty, discomfort, or time involved in conventional techniques for anesthetizing the sphenopalatine ganglion are not practical for an ED setting and may be preventing study of this treatment.

A recently Food and Drug Administration–cleared device (Tx360; Tian Medical LLC, Lombard, IL) may facilitate the procedure of anesthetizing this ganglion. This device is designed to position a flexible microcatheter, inserted through the nares, in close proximity to the ganglia in the posterior nasopharynx (Figure 1). At the tip of this catheter, a small delivery port is engineered to directionally spray the medication superiorly, laterally, and anteriorly to the sphenopalatine ganglion. The procedure takes as little as 10 seconds per side to perform in awake patients who remain seated during the procedure.[19] If effective for acute headache, sphenopalatine ganglion block using this technique could be a feasible alternative to conventional therapies in the ED.

Goals of This Investigation

The objective of this study was to evaluate the efficacy of sphenopalatine ganglion block with the Tx360 device for the treatment of acute frontal headache in patients presenting to the ED. Our hypothesis was that bupivacaine delivered to the sphenopalatine ganglion would achieve a 50% reduction in acute anterior headache pain in a greater proportion of patients than normal saline solution placebo delivered in the same manner.

MATERIALS AND METHODS

Study Design and Setting

We conducted a randomized, double-blind, placebo-controlled trial in 2 urban EDs. Both EDs are academic Level I trauma centers with an annual census of 100,000 to 110,000 patients per year. We enrolled eligible patients in a convenience sample from October 1, 2012, to December 1, 2013, according to research assistant coverage. The study was approved by the institutional review board of Indiana University School of Medicine. This study is reported in accordance with Consolidated Standards of Reporting Trials (CONSORT) guidelines.

Selection of Participants

Patients aged 18 to 65 years were eligible if they presented to the ED with a frontal-based crescendo-onset headache and a normal neurologic examination result.

Frontal-based headache was defined as affecting the frontal, temporal, orbital, maxillary, or mandibular region. Specific classification of the type of headache was not attempted or required for enrollment. Patients gave consent for participation to a research assistant, and formal written informed consent was obtained.

Patients with headaches that originate in the posterior or occipital region were excluded because anesthesia of the sphenopalatine ganglion is less likely to affect these headaches, according to the theorized mechanism of action. Patients were also excluded if they had a temperature greater than 37.7°C (100°F), had signs of acute or chronic sinusitis, exhibited nuchal rigidity, or had sudden-onset headache. Other exclusion criteria included self-medication for headache with pain or antinausea medication within 4 hours preceding enrollment; bleeding diatheses; pregnancy; peripheral vascular disease; cancer; HIV; history of nasal insufflation of illicit drugs; nasal septal deformity; recent nasal or sinus surgery; nasal passage dryness, soreness, oozing, or bleeding; allergy to local anesthetics; participation in another investigational trial within the preceding 30 days; or lack of telephone for follow-up contact.

Interventions

Patients who qualified for the study were randomly assigned in a 1:1 ratio with a computer-generated randomization schedule to receive either 0.5% bupivacaine or normal saline solution. The central hospital pharmacist prepared a 1-mL syringe with either the bupivacaine or the saline solution according to the randomization schedule and delivered the blinded medication to the research assistant or treating physician. Both the bupivacaine and the saline solution were identical in odor, clarity, color, and consistency. The delivery of the medication to the patient was thus conducted in a blinded fashion.

Using the Tx360 device, a trained physician administered 0.3 mL of the assigned medication transnasally to the bilateral posterior nasopharynx in accordance with the device manufacturer's instructions (http://tianmedical.com/Tx360.asp). The device is designed to be positioned in the anterior nasopharynx, aimed slightly medial and inferior, with the catheter retracted within the device. Once positioned, the catheter is advanced from within the device into the open space of the nasopharynx. The syringe is turned laterally, which positions the catheter opening at the location of the sphenopalatine ganglion (Figure 1). The plunger on the syringe is then pushed to deliver 0.3 mL of the medication. Bilateral sphenopalatine ganglia are treated regardless of any laterality of symptoms.

Training for the treating physician required a brief (<10-minute) tutorial on how to use the device. Training was delivered by another trained physician or a video on the manufacturer's Web page. During the course of the study, 17 physicians used the device at least once. None of the physicians required any retraining, but all had access to the manufacture's Web site, pamphlet, and video, and to the research assistants, who also went through the training.

If after 15 minutes the patients believed that they required further treatment, the decision was left up to the discretion of the treating physician. At our institution, the most common headache therapies currently are intravenous prochlorperazine and metoclopramide.

Methods of Measurement

Pain assessment occurred at 0 (baseline), 5, and 15 minutes. Patients requiring additional treatment for headache after 15 minutes were offered rescue treatment for headache or nausea in the ED at the discretion of the treating physician. We measured pain and nausea through 100-mm, unnumbered, horizontal, visual analog scales. The research assistant or investigator completed 24-hour follow-up with the patient through a telephone call assessing pain and nausea by a 0- to 10-point Likert scale and assessed any further symptoms, adverse effects, and return to normal daily activities.

The research assistant collected data on paper forms at the times specified. The patients themselves marked the 100-mm visual analog scale to rate their pain and nausea at the times specified. At the completion of the ED visit, the research assistant measured the visual analog scale and entered the study data into a research electronic data capture tool hosted at our academic institution for data management.[20] The tool is a secure, Web-based application designed to support data capture for research studies.

Outcomes Measures

The predefined primary endpoint was a 50% absolute pain reduction on a 100-mm visual analog scale at 15 minutes. We compared the absolute risk difference between the percentage of subjects in each group achieving this primary endpoint.

Secondary outcomes included reduction of pain by greater than 19 mm on the visual analog scale as a minimally significant reduction in pain, nausea reduction, and percentage of patients who were pain and nausea free at 15 minutes. At 24-hour follow-up, we compared the medians of the Likert scale responses for both pain and nausea. We also compared the percentage of patients who were pain and nausea free at 24 hours. Any adverse events were recorded, and we assessed nasopharyngeal and other adverse effects at 24-hour follow-up as well.

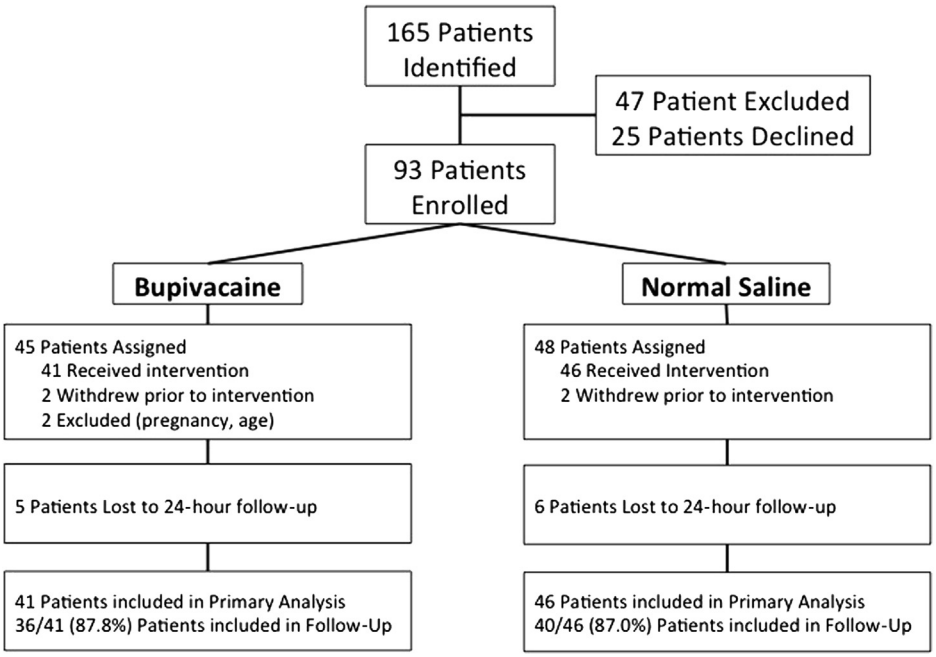

Figure 2. CONSORT flow diagram for enrollment in the trial.

Primary Data Analysis

A power calculation was completed before the start of enrollment. The trial was designed to evaluate the superiority of bupivacaine to normal saline solution as delivered by the method described. Assuming a 2-sided α of .05, we calculated that 84 patients were necessary to achieve 80% power to detect a difference of 30% (30% meeting the primary endpoint for placebo versus 60% for bupivacaine) of patients between the 2 groups meeting the primary endpoint. We performed a χ^2 test to assess the difference in the primary endpoint between the 2 groups. Additionally, we used the Wilcoxon rank sum test to compare continuous secondary endpoints and demographic characteristics between the 2 groups. χ^2 Tests were used to compare dichotomous secondary endpoints and categorical demographic characteristics between the 2 groups. Analyses were performed with SAS (version 9.3) and SigmaPlot (version 12.5). Graphing of visual analog scale data and Likert scale dot density plots was performed with SigmaPlot (version 12.5).

Table 1. Groups at baseline.

Characteristics	Bupivacaine (n=41)	Saline Solution (n=46)
% Female	75.6	71.7
Median age (IQR), y	33 (23–44)	41 (29.25–51)
Median baseline headache score (IQR), mm	80 (66–93)	78.5 (64–91.75)
Median baseline nausea score (IQR), mm	29 (0–48)	0 (0–45.5)

IQR, Interquartile range.

RESULTS

Characteristics of Study Subjects

Of 165 patients identified between October 1, 2012, and December 10, 2013, we enrolled 93. Four patients withdrew from the study before receiving the study drug or placebo through the device. Three of these patients stated they were anxious about the device or its delivery mechanism, and the fourth stated after enrollment that he "might be allergic." Two patients were excluded after randomization: one patient was found to be pregnant after randomization and another patient was enrolled outside of the age range exclusions. These 6 patients were not included in the primary analysis; however, we completed a sensitivity analysis with intention-to-treat principles, and this is reported as well. Of the remaining patients, 41 were randomized to receive bupivacaine, and 46 were randomized to receive saline solution (Figure 2). The 2 groups were similar in terms of sex, baseline headache score, and baseline nausea score. Although the range of ages was similar between the 2 groups, the median age of the bupivacaine group (33 years) was younger than that of the normal saline solution group (41 years) (Table 1).

Main Results

For the primary outcome, there was no difference between the 2 groups for the percentage of patients achieving a 50% reduction in headache score at 15 minutes (Table 2). The risk difference was 7.5% (95% confidence interval [CI] –13% to 27.1%). Figure 3 shows medians and

Table 2. Results: headache and nausea at 15 minutes.

Outcome Measure	Bupivacaine	Saline Solution	Difference, %	95% CI
15 min	N=41	N=46		
50% reduction in mm VAS, No. (%)	20 (48.8)	19 (41.3)	7.5	−13.0 to 27.1
>19 mm VAS reduction, No. (%)	25 (61.0)	23 (50.0)	11.0	−9.6 to 30.3
Headache free (%)	11 (26.8)	12 (26.1)	0.7	−17.0 to 19.0
Nausea free (%)	30 (73.0)	32 (69.5)	3.5	−15.3 to 21.8
Discharged without rescue medications (%)	18 (43.9)	17 (37.0)	6.9	−13.0 to 26.5
Median headache score (IQR), mm VAS	34 (6 to 78)	51.5 (10 to 73.5)	17.5	−15.2 to 50.2
Median nausea score (IQR), mm VAS	0 (0 to 4)	0 (0 to 7.25)	0	−0.5 to 5

VAS, Visual analog scale.

interquartile ranges for each group at baseline and at 15 minutes. Also included are the individual patient data pre- and postintervention, with a line connecting their baseline and 15-minute visual analog scale scores. We analyzed the data with an intention-to-treat analysis for the patients who dropped out before study medication delivery and for those who were excluded after randomization. This analysis using a best- or worst-case scenario would not have changed the significance of the results for the primary endpoint.

Among the secondary outcomes, there was no difference in patients reporting any ongoing headache at 15 minutes (risk difference=0.7%; 95% CI –17.0% to 19.0%). The percent of patients who were nausea free at 15 minutes was also similar between the groups (risk difference=3.5%; 95% CI –15.3% to 21.8%). Patients were discharged without rescue medication after the 15-minute endpoint in 43.9% of bupivacaine patients and 37.0% of saline solution patients (risk difference=6.9%; 95% CI –13.0% to 26.5%). There was no difference in the median headache scores on the visual analog scale at 15 minutes.

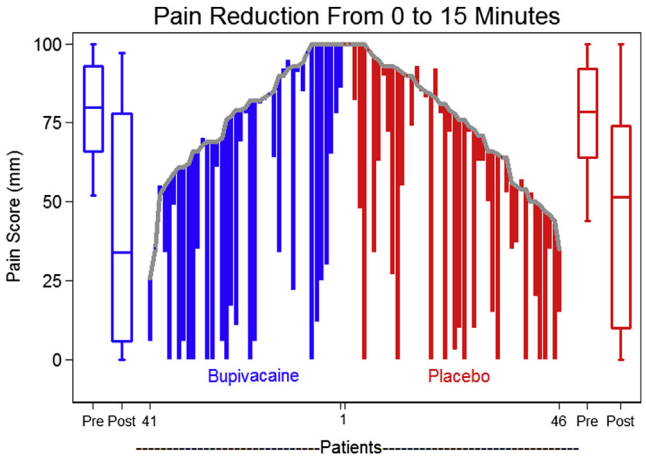

Figure 3. Box plots show median and interquartile ranges for baseline (pre) and 15-minute (post) headache scores on a 100-mm visual analog scale. The individual patient response to therapy for each group is also displayed.

Next-day follow-up was achieved for 76 patients, 36 (87.8%) randomized to bupivacaine and 40 (87.0%) randomized to saline solution (Table 3). At 24 hours, 72.2% of the bupivacaine-treated and 47.5% of the saline solution–treated patients were headache free, representing a risk difference of 24.7% (95% CI 2.6% to 43.6%). No nausea was present in 94.4% versus 77.5% of patients, with a risk difference of 16.9% (95% CI 0.8% to 32.5%). The median 24-hour headache score (measured on a 10-point scale) was lower in the bupivacaine group (0 versus 1; interquartile range 0 to 1.25 versus 0 to 7). Figure 4 shows the medians and interquartile ranges of headache scores at 24-hour follow-up for all patients for whom follow-up was achieved, as well as for those who did receive rescue medications during their index visit.

We performed a post hoc sensitivity analysis, assuming a worst-case scenario for the secondary endpoint of 24-hour headache free. In a worst-case scenario (assuming all patients in both groups lost to follow-up were not headache free at 24 hours), the overall risk difference was 22.1% (95% CI 1.6% to 42.6%). Of the patients who did not require any rescue medication and for whom 24-hour follow-up was achieved, 88.2% (15/17 patients) versus 56.2% (9/16 patients) were headache free at 24 hours, with a risk difference of 32.0% (95% CI 1.4% to 56.6%).

Patients reported few adverse effects at 24 hours. Nasopharyngeal symptoms were reported by 5 of 36 patients (13.9%) in the bupivacaine group, and 3 of 40 (7.5%) in the saline solution group reported at the 24-hour follow-up, an absolute risk difference of 6.4% (95% CI –8.2% to 22.0%). The symptoms reported were "nasal dryness," "runny nose," "sore throat before going to bed," "congestion pre and post," and "hoarseness" in the bupivacaine group; and "slight nosebleed," "slight runny nose," and "minor bloody nose in the morning" in the saline solution group. No severe adverse events were reported in either group during the ED stay or at 24-hour follow-up.

Table 3. Results: headache and nausea at 24-hour follow-up.

Outcome Measure	Bupivacaine	Saline Solution	Difference, %	95% CI
24 h	N=36	N=40		
Headache free (%)	26 (72.2)	19 (47.5)	24.7	2.6 to 43.6
Nausea free (%)	34 (94.4)	31 (77.5)	16.9	0.8 to 32.5
Median headache score, 0–10 Likert (IQR)	0 (0 to 1.25)	1 (0 to 7)	1	−1.4 to 3.4
Median nausea score, 0–10 Likert (IQR)	0 (0 to 0)	0 (0 to 0)	0	0 to 0
24 h: patients without rescue medications	N=17	N=16		
Headache free (%)	15 (88.2)	9 (56.2)	32.0	1.4 to 56.6
Nausea free (%)	17 (100)	14 (87.5)	12.5	8.0 to 36.0
Median headache score, 0–10 Likert (IQR)	0 (0 to 0)	0 (0 to 5.25)	0	−2.1 to 2.1
Median nausea score, 0–10 Likert (IQR)	0 (0 to 0)	0 (0 to 0)	0	0 to 0

LIMITATIONS

There are limitations to this study. We measured headache severity up until 15 minutes and at 24-hour follow-up. It is unclear whether sphenopalatine ganglion block might have shown a benefit at some point after 15 minutes but still during the initial ED encounter. In retrospect, a 1- or 2-hour assessment would have allowed a better determination of when the responses to the 2 treatments became divergent. If no difference was apparent until 24 hours, then sphenopalatine ganglion block would not be a particularly useful single agent for most ED headache patients, but headache relief at 1 hour would be clinically important to patients and emergency practitioners. When the study protocol was developed, the timeframe of 15 minutes for efficacy of a sphenopalatine ganglion block was selected according to previous studies.[12,19] However, bupivacaine as an agent for nerve block can be slow to absorb and take effect, and this should have been taken into account. Future studies should assess initial headache response during a longer initial timeframe.

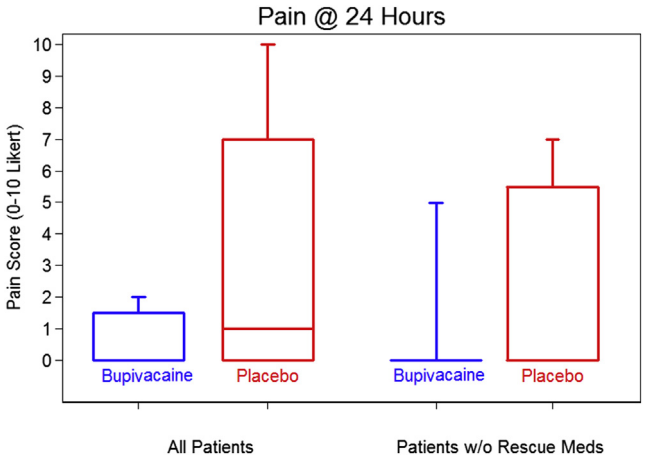

Figure 4. Headache at 24-hour follow-up. Box plots show median and interquartile ranges for Likert score (0 to 10) for all patients for whom follow-up was obtained and for the group that did not receive rescue medicines after the intervention.

The median age of the bupivacaine group was 8 years younger than that of the saline solution–treated group. The age difference did not reach statistical significance and the age ranges in the 2 groups are similar. We are unaware of any clinical or pathophysiologic evidence to suggest that there would be a difference in headache response according to age. We completed a logistic regression analysis to adjust for the difference in age between groups, which did not significantly change the results for the primary endpoint.

There was the potential for unblinding. Although the medications were identical in many ways, bupivacaine and saline solution are different in taste and the production of anesthesia. The small volume of medication, as well as the localized spray, should limit the amount of medication available to the oropharynx, but there is the potential for anesthetic to create an identifiable taste and unblind the patient. Both bupivacaine and saline solution have a noxious taste and most patients have had no experience with which to compare the two. It is unclear what effect the potential for unblinding of patients would have had in our study. Given the relatively impressive therapeutic response in the saline solution–treated patients, it seems unlikely that unblinding, if it occurred, produced any significant effect.

Approximately 13% of our patients were lost to 24-hour follow-up. The number of patients lost to follow-up was similar in the 2 arms of the study. A post hoc sensitivity analysis found that this would not have significantly altered the 24-hour secondary outcomes.

We found that both bupivacaine and saline solution sphenopalatine ganglion block produced complete headache resolution in 26% of patients at 15 minutes, and that either treatment produced a 50% reduction in headache at 15 minutes in greater than 40% of patients. Although a substantial placebo effect is common in studies of headache therapy, these results are impressive for a true placebo.[21,22] It is possible that the sphenopalatine ganglion was stimulated mechanically because of the pressure of the spray or even by the absorption of saline solution itself,

producing a therapeutic effect. Using a sham device that sprays to a different location than the sphenopalatine ganglion may be a better control for assessing a difference between groups.

The findings of benefits at 24 hours were secondary outcomes and need to be validated in further studies. Although the 24-hour results showed consistent benefit with bupivacaine sphenopalatine ganglion block, we assessed multiple secondary endpoints, increasing the possibility of finding differences caused by chance alone.

Last, this was a relatively small study conducted at 2 academic EDs associated with a single teaching institution. Future work will be needed to determine whether these results are reproducible in other clinical environments.

DISCUSSION

We completed a double-blind, randomized trial of sphenopalatine ganglion block in the ED, using bupivacaine delivered by the Tx360 device. In this study, bupivacaine was not shown to have an immediate benefit over normal saline solution placebo for the primary outcome of a greater than or equal to 50% reduction in headache severity at 15 minutes. The bupivacaine group also did not show benefits in the secondary outcomes assessed at the 15-minute interval.

The finding of no immediate benefit is surprising, given the proposed mechanism of action of sphenopalatine ganglion block, as well as the results from Maizels and Geiger.[12] These authors demonstrated an immediate benefit of sphenopalatine ganglion block for migraine treatment with conventional transnasal approach of topically dripped lidocaine versus saline solution in a recumbent patient. There are several possible explanations about why this might have occurred in our study. One explanation is that sphenopalatine ganglion block with bupivacaine may take longer than 15 minutes to have the desired effect in some patients. For the primary outcome, we did not assess the timeframe beyond the initial 15 minutes after study drug delivery, the reasoning being that rescue medications would confound any outcomes after that. The majority of patients in both groups received rescue medication after the 15-minute efficacy assessment. This study may have benefited from a longer primary outcome assessment.

Another explanation may be the size of the placebo effect in this study. More than 40% in each group had a significant reduction in headache at the primary endpoint of 15 minutes. Placebo effect has been well documented in headache trials; however, these are still striking results to be achieved with a true placebo in only 15 minutes.[21,22] Half of the patients in the placebo group versus 61% in the bupivacaine group had a 20-mm or greater reduction in headache at 15 minutes. More than 26% of patients in both the bupivacaine group and the saline solution group reported complete resolution of headache at 15 minutes. And maybe most important to emergency physicians, 43.9% of the bupivacaine group and 37% of the placebo group were able to be discharged from the ED after the 15-minute time from drug delivery, without further treatment.

Given the design of our study, it is possible that stimulation of the sphenopalatine ganglion in the placebo group produced a short-lived reduction in headache symptoms, whereas bupivacaine acts to produce a more lasting effect because of its anesthetic properties. It is believed that other forms of stimulation of the sphenopalatine ganglion, such as electrical, can abort headache.[11,23] Thus, it is possible that mechanical stimulation of the sphenopalatine ganglion by the spray of saline solution or chemical changes in the ganglion from the absorption of saline solution itself resulted in some benefit. To test these hypotheses, a better sham could be designed.

Despite the finding of no immediate difference between bupivacaine and placebo, at 24 hours more patients in the bupivacaine group were headache free and nausea free than in the placebo group. This finding may lend support to some of the theories above, but confirming or refuting benefit at 24 hours will require further study. This study was not designed or powered to specifically examine this outcome, so it is possible that we simply experienced a type I error. There is also the possibility that sphenopalatine ganglion block has some effect when used independently but works synergistically with dopamine antagonists, our typical rescue agents, to have a stronger effect. Although there was no difference in the outcomes measured before rescue medication at 15 minutes, there were apparent differences by 24 hours, after rescue medications had been offered. It is unclear when the apparent efficacy in the 2 treatment arms became divergent. Although synergy is a possibility, it seems unlikely to completely explain the results, given the finding that the 24-hour benefit appeared to be sustained in patients who did not receive rescue medications. Given these findings, the possibility remains that sphenopalatine ganglion block with this device has a role in the treatment of acute anterior headache in the ED.

There are some important questions raised by these data for future study. One is whether mechanical stimulation of the sphenopalatine ganglion plays a role in the early relief of headache. A related question is the suggestion by the 24-hour outcomes that there is a prolonged effect of

bupivacaine versus saline solution. A third question is the synergistic role of sphenopalatine ganglion block along with conventional therapy. In retrospect, a better sham might have been designed to act as control for sphenopalatine ganglion block in this study and would be important to develop for future trials.

In conclusion, sphenopalatine ganglion block with the Tx360 device with bupivacaine did not result in a significant increase in the proportion of patients achieving the primary outcome of a greater than or equal to 50% reduction in headache severity at 15 minutes compared with saline solution applied in the same manner. However, several questions were raised in this study and warrant further trials to evaluate the role of sphenopalatine block in acute headache care in the ED.

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Author affiliations: From the Department of Emergency Medicine (Schaffer, Hunter, Weaver), Indiana University School of Medicine (Ball), Indianapolis, IN.

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